GCGCCCCCTGAGCAGAAAACAGGAAGAACCAGGCTCGGTCCAGTGGCACCCAGCTCCCTACCTCCTGTGCCAGCCGCCTGGCCTGTGGCA 180 1 sma CCTCTCTGGTTTCCTGGCGCCCATTTCACGGCTGTGATTCTGCTGAGGAACTTCCCCGGGTGAGCCCCGGCTTCCTCCGAGCCTGGCACC 360 S L Y S W R A F H G C D S A E E L F R V S P R F L R A W H Sma I CCCCTCCCGTCTCAGCCAGGATGCCAACGAGGCCCCTGGGCCCCCGGGCACCCCAGTGTATCACCAAATGCGAGCACACCCGCCCCAAGCCAG 450 PGTGCITKCEHTRPKP $\mathbb{Z}_{\mathsf{pdgagctggccttccgcaagggcgacgtggtcaccatcctggaggcctgcgagaacaagagctggtaccgcgtcaagcaccaccactg 540 <math>\mathbb{SH}_{\mathbb{Z}}$ ELAFRKGDVVTILEACENKSWYRVKHHTS GACAGGAGGGCCTGCTGGCAGCTGGGGCCCTGCGGGAGCGGGAGGCCCTCTCCCCAGACCCCAAGCTCAGCCTCATGCCGTGGTTCCACG 630 GOEGLLAAGALREREALIS 1 S G Q E A V Q Q L Q P P E D G L F L V R E S A R H P G ACTACCTCCTGTGCCTCAGCTTTGGCCGCGACGTCATCCACTACCGCGTGCTGCACCGCGACGGCCACCTCACAATCGATGAGGCCGTGT 810 DYVLCVSFGRDVIHYRVLHRDGHLTIDEAV TCTTCTGCAACCTCATGGACATGGTGGAGCATTACAGCAAGGACAAGGGGCGCTATCTGCACCAAGCTGGTGAGACCAAAGCGGAAACACG 800 FCNLHOHVEHYSKOKGAICTKLVRFKRKH OHLTLGAQIGEG C T K S A E E E L A R A G W L L N L Stu i AGTTTGGAGCTCTCCTGCAGGCTGAGTACCTGGGGCAAAAGGTGGCCGTGAAGAATATCAAGTGTGATGACAGCCCAGGCCTTCCTGG 1080 EFGAVLOGEYLGOKVAVKNIKCOVTAQAF ACGAGACGGCCGTCATGACGAAGATGCAACACGAGAACCTGGTGCGTCTCCTGGGCGTGATCCTGCACCAGGGGCTGTACATTGTCATGG 1170 DETAVHTKHQHENLVRLLQVILHQQLYIVH Psti Sma I AGCACGTGAGCAAGGGCAACCTGGTGAACTTTCTGCGGACCCGGGGGTCGAGCCCTCGTGAACACCGCTCAGCTCCTGCAGTTTTCTCTGC 1260 EHVSKGNLVNFLRTRGRALVNTAQLLQFSL

FIGURE 1A

CTCAAACAC L K H CCCTAAAATC P K H	S D F G CCCGGAACTTCACC G G K F T CCTCACTGAAAGAG S L K E	CAGCAAGTCGGATGT	E R K G 1 TCTGGAGTTTTG	Nde I GGTGCTGCTCTGGGAGGTCTTCTCATATGGAC V L L V E V F S Y G Kon I ACCGCATGGAACCCCCCGAGGGCTGTCCAGGCC	eggcTCCGT
CCTCAAAATC PKH	S D F G CCCGGAACTTCACC G G K F T CCTCACTGAAAGAG S L K E	CAGCAAGTCGGATGT	E R K G 1 TCTGGAGTTTTG	DSSRLPVKWT Nde I GGTGCTGCTCTGGGAGGTCTTCTCATATGGAC VLLVEVFSYG Kon I ACCGCATGGAACCCCCCGAGGGCTGTCCAGGCC	GGGCTCCGT 1
CCCTAAAATG PKH	CCCGGAAGTTCACC 1 G K F T 1 G K F T 1 G K F T 1 G K F T 1 G K E	CAGCAAGTCGGATGT S K S D 1	TCTGCAGTTTTG V V S F TCGAGAAGGGGT	Nde I GGTGCTGCTCTGGGAGGTCTTCTCATATGGAC V L L V E V F S Y G Kon I ACCGCATGGAACCCCCCGAGGGCTGTCCAGGCC	CCCCT 1
CCCTAAAATG	G K F T	S K S D '	Y W S F	GGTGCTGCTCTGGGAGGTCTTCTCATATGGAC V L L V E V F S Y G Kon I ACCGCATGGAACCCCCCGAGGGCTGTCCAGGCC	R A P
CCCTAAAATG PKH	G K F T	S K S D '	Y W S F	KON I ACCGCATGGAACCCCCCGAGGGCTGTCCAGGCC	R A P
CCCTAAAATG P K H	G K F T	S K S D '	Y W S F	KON I ACCGCATGGAACCCCCCGAGGGCTGTCCAGGCC	R A P
CCCTAAAATC P K H	TETCACTEAAAGAG 1 S L K E	EGTGTCEGAGGCCG		I ACCGCATGGAACCCCCCGAGGCCTGTCCAGGCC	CCCTCCACE
P K H	SLKE			I ACCGCATGGAACCCCCCGAGGCCTGTCCAGGCC	CCCTGCACG
P K H	SLKE			I ACCGCATGGAACCCCCCGAGGCCTGTCCAGGCC	CCCTCCACC
P K H	SLKE			ACCREMI MBWWOOOGGATUGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	CCCTCCACC
P K H	SLKE				
73			YEKG	YRHEPPEGCPG	PVH
77				01	
17	Pvu II			Sma I	
479	CACCTGCTCGGAC	GCAGAGCCCGCCC	ECCGGCCACCCT	TCCGCAAACTGGCCGAGAAGCTGGCCCGGGAGC	TACCCAGTC
	S C Y E	A E PIA	RRPP	FRKLAEKLJARE	L R S
LHS			A MATE		
ACSTGCCCC	CAGCCTCCGTCTC	AGGGCAGGACGCCG	ACCCCTCCACCT	COCCCGAAGCCAGGAGCCCTGACCCCACCCG	TOOOSOS
GAP	•	A Q D A	D G S T -	SPRSOEP. 1	
	•				
FEGCCCCAGA					
[CCCCACAGC	AGUALLUAGAGAGAG	TCGAGAGTGCGGCG	TEGGGGCACTGA	CCAGGCCCAAGGAGGGTCCAGGCGGGCAAGTC	ATCCTCCTGG

V D R D L C V K V S D F G M T R Y V L D D Q Y V S S V G T K

FIGURE 2B

CCCGACTGGTCGAAAGACAGGAACAGACTTGAAACAGGGGGAGAGCTCCTGGCGAAACGAAGACGTGGAGGTTTTACCAGGGATAAGAAG 90 TCTCTCCAGGTAGGACTTGCTGCAACCCAGCTGCTGGACTGATCTGAAACGGGACTTTGCATACTCTCCGAAGTATGGTGAGTTGGTGCT 270 CACTTCAAAGTTGCCTGGTGAAGGAAGATAAGGTGGATCGCAGAGACTAAGGGGAGAGGGGAGAAGCCCTGCTCCTCTTCTCCCCAACAAG 360 GCACANTEAGCAACATCTGTCAGAGGCTCTGGGAGTACCTAGAACCCTATCTCCCCTGTTTGTCCACGGAGGCAGACAAGTCAACCGTGA 450 M S N I C O R L W E Y L E P Y L P C L S T E A D K S T V I ENPGAL C SPOSORH GHY FV (A L F D Y Q A R T AGGACTTGAGCTTCCGAGCAGGTGACAAACTTCAAGTTCTGGACACTTTGCATGAGGGCTGCTGCTTTGCCAGACACTTGGAGAAAAGAC 630 SH 3 EDLSFRAGDKLQ V L D T L H E G W W F A R H L E K R GAGATGGCTCCAGTCAGCAACTACAAGGCTATATTCCTTCTAACTACGTGGCTGAGGACAGAAGCCTACAGGCAGAGCCGTGGTTCTTTG 720 D G S S Q Q L Q G Y I P S N Y V A E D R S L Q A E P W F F. GACCAATCGGAAGATCAGATGCAGAGAAACAACTATTATATTCAGAAAACAAGACCGGTTCCTTTCTAATCAGAGAAAGTGAAAGCCAAA 810 A I G R S D A E K O L L Y S E N K T G S F L I R E S E S O SHA K G E F S L S V L D G A V Y K H Y R I K R L D E G G F F L T GAAGAAGAATCTTTTCAACACTGAACGAATTTGTGAGCCACTACACCAAGACAAGTGACGCCTGTGTGTCAAGCTGGGGAAACCATGCT 990 SDGLCVKLGKPC RRRIFSTLNEFVSH PBOL SDAADTCCAGCTCCAGCTCCATTGACTTGTCGTATAAACCGTGGACCAATGGGAGATAGACCGCAACTCCATACAGCTTCTGAACA 1080 LKIQVPAPFDLSYKTVDQVEIDRNSIQLLK CATTGGCATCTGGTCAGTTTGGCGAAGTATGGGAAGGTCTGTGGAACAATACCACTCCAGTAGCAGTGAAAACATTAAAACCAGGTTCAA 1170 R L <u>G S G Q F G E V W E G L W N N T T P Y A V K T L K P G S</u> TEGATCCAAATGACTTCCTGAGGGAGGCACAGATAATGAAGAACCTAAGACATCCAAAGCTTATCCAGCTTTATGCTGTTTGCACTTTAG 1260 M D P N D F L R E A Q I H K N L R H P K L I Q L Y A V C T L AAGATCCAATTTATATTACAGAGTTGATGAGACATGGAAGTCTGCAAGAATATCTCCAAAATGACACTGGATCAAAAATCCATCTGA 1350 EDPIYITELMRHGSLQEYLQNDTGSKIHL CTCAACAGGTAGACATGGCGGCACAGGTTGCCTCTGGAATGGCCTATCTGGAGTCTCGGAACTACATTCACAGAGATCTGGCTGCCAGAA 1440 Q Q V D H A A Q V A S G M A Y L E S R N Y I H R D L A A R ATGTCCTCGTTGGTGAACATAATATCTACAAAGTAGCAGATTTTGGACTTGCCAGAGTTTTTAAGGTAGATAATGAAGACATCTATGAAT 1530 Y L V G E H N I Y K V A D F G L A R V F K V D N E D I Y E CTAGACACGAAATAAAGCTGCCGGTGAAGTGGACTGCGCCCGAAGCCATTCGTAGTAATAAATTCAGCATTAAGTCCGATGTATGGTCAT 1820 SRHEIKLPYKWTAPEAIRSNKFSIKSDVW3 TTGGAATCCTTCTTTATGAAATCATTACTTATGGCAAAATGCCTTACAGTGGTATGACAGGTGCCCAGGTAATCCAGATGTTGGCTCAAA 1710 I T Y G K H P Y S C H T C A Q Y I Q H L A O ACTATAGACTTCCGCAACCATCCAACTGTCCACAGCAATTTTACAACATCATGTTGGAGTGCTGGAATGCAGAGCCTAAGGAACGACCTA 1800 NYRLPQPSNCPQQFYNIKLECVNAEPKERP

F. M. A.

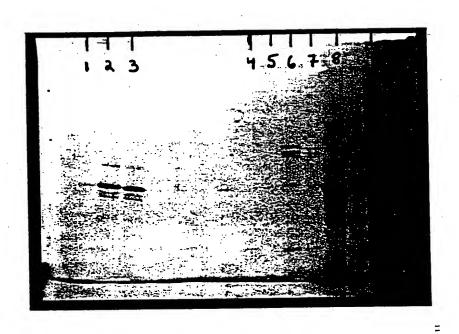
Į.i.

FIGURE 3B

Expression of MKK1 and MKK2

		MKK1	MKK2
Human	<u>l</u>		1
	Meg-01	+++	+++
Meg/Eryth	K562	++	+
	Mo7e	++	+
	HEL	+++	++
. 9	KG-1	+	++
Myelo/Mac	HL-60	+	+
	TF-1	+	+
B-cell	ALL-1		+
	Raji	•	• .
	Daudi	-	•
	Molt-3	-	- ·
T-cell	Jurkat	•	- ·
Epithelial	Hela	• ·	•
Roden	t	· ·	
	BM	+	+++
	Spleen	+++	+
	Thymus	-	-
	Liver	•	
	Brain	+	÷ -
rat neural	P19	+	- · .

Immunoprecipitation Of In Vitro Transcribed Translated MKK1 And MKK2 Proteins



Antisense MKK1 Expression Suppresses AChE Production In Primary Murine Bone Marrow Cultures

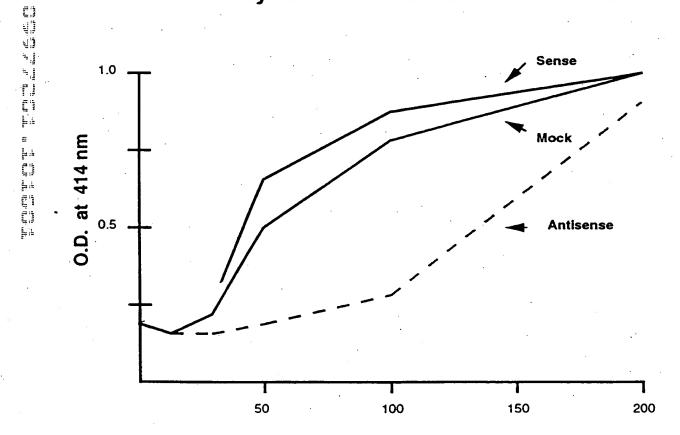
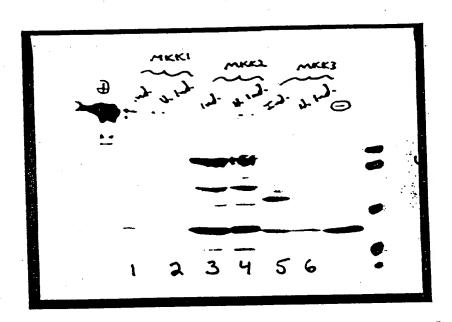


FIGURE 6A

Cell Number x 10³/200 ul

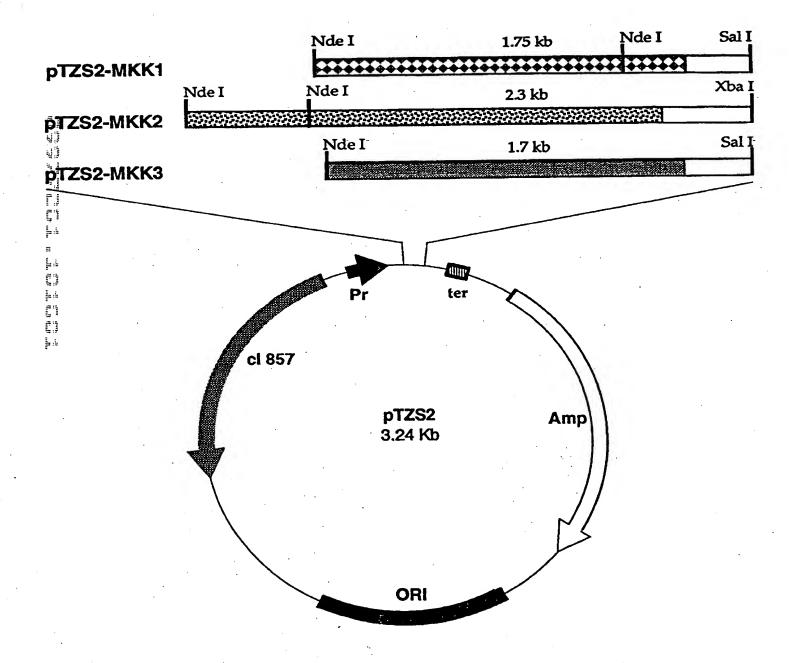


FIGURE 6B



offer ging man bene dien bene bene die Gene

The deal strate that their the



1	M A C	RO	G S Q A	L A	v <u>s</u>	W -	R Λ	F -	H -	<u>G</u> C	<u> </u>) S	. A	E -	E	L -	P -	R	v :	S	P F	F	L -	h(CK1 CSK	aa (C	і лн055	9)	
31 · 8	RAV	Н :	P P	P -	<u>v s</u>	<u>A</u>	R M	P	T	R I	₹ ¥ - \v	V E	· P	ြင	T	O	C C	I	T A	K (C F	I F	T H	MI h(CK1 CSK	aa (J	а JH055	9)	
61 22	RPF	E	G E Q D	L	A F P F	R	K G	D D	v V	V L	r :	ון <i>י</i>	E	X V	C	E	N D	K P	s N	W.	Y I	R \	k k	MI h	KK1 CSK	aa (,	а JH055	9)	
52	HHT	7 - L	G R	E	G I	Ι	PLA	N	Y	V	Q I	KLI	R E	ij G	V	K	A	G	тĮ	<u>K</u>	<u>L:</u>	S Į	, <u>M</u>	l Do	CSK	(,	JHUDE	59)	
121 81	P W I	F H F H	G K	I	S C	OE	E A) E	O R	O L	<u>ار</u> د	ן אַ	P I	E	T	G	L L	F F	L L	V V	R I	E :	A S] M	KK1 CSK	a. (,	а JH055	59)	
151 111	RH	P G	D Y D Y	V T	L C	: V : V	s i	G D	R	D K	v V	I I	H 3	/ F	V V	L M	H Y	R	D A	G S	H K	ני נו	r I SlI	M h	KK1 CSK	a (а JH05!	59)	
181 141	D E	A V E V	F F Y F	C E	N I	M M	D I	v LV	E	H H	Y Y	S :	K I	O P	C G) G	I L	c lc	T T	K	r)	V I	R P	M h	KK1 CSK	a (а JH05!	59)	
171	K R K V	K H M E	G T	V	S A	A E	E I	E L E F	Y	R R	A Sl	G '	W .	I J	. N	I L	O K	H	L	T	L	G L	A O] M h	IKK1 ICSK	. a	а (JH05	59)	
241 201	I G	E G KlG	E F	G	A V	V L	O L	G E	Y	E R	င င	O N	K K	V 1	7	/ K	C	I	K K	C	D D	V A	T A	l l	IKK1 ICSK	. ā	а (J Н05	ŝ9)	
231		F L	D E	TA	A S	V M	T T	K M	1 O	H	E S	N	L L	v i	R I	LI	G G	v v	I	L V	H	O E	 K (- N	IKK1 nCSK		аа (JH05	59)	
299 261	GL	Y I Y I	v v	1 E	H Y	V S	K K	G 1	I L	v v	N D	F Y	L L	R R	r I	R C	; F	ξ <u>A</u>	L V	V L	N G	T G	A C		MKK] nCSI	L a	аа (JH05	59)	
329 291	LL	O F K F	S I	L D	V V	A E	G	M I	E Y	L	E E	S	K N	K N	L F	V I	1 F	? E	L	A	A	R R	N V	V	MKK hCSI	L a	аа (JH05	559)	
359 321	LV	S E S E	D I	บ V N V	A	ΚV	7 S	D I	F C	L	A	K K	A	E A	R S	K (G I		S	S G	R	L	P '	V V	MKK hCS	1 K	aa (JH0	559)	
389 351	K W	T A	P	E A	L	K I	I G E K	K K	F ?	r s	K K	s s	D D	V V	W	s s	F (G G		, I	. W	E	V	F Y	MKK hCS	1 K	аа (JH0	559)	
419 38	9 S <u>Y</u> 1 S F	G F	Ā	P \	P P	K I	M S I P	L L	K I	E V	' S ' V	E	A	v lv	E E	K K	G G	Y]	R N KL	1 E	E P	P	E	G G	MKK hCS	1 K	aa (JH0	559)	
44	9 C P	G F	\V	H V	V L E V	M M	S S K N	c lc	W W	E A	E	P	A	R	R R	P P	P S	F :	R I	2 L	F	E	K Q	L L	MKK	CI SK	aa (JH0	559)	
47	9 A R	E I	R	s .	A G	A	P A	<u>s</u>	V I	S C	3 C) D	A L	D	G -	<u>s</u>	T -	<u>s</u>	P !	R :	s C) E	P -	L	MKE			559)	

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MDTKSILEELLLKRSQQKKKMSPNNYKERL MKK2 aa
MAA-VILESIFLKRSQQKKKTSPLNFKKRL hAtk (X58957)
MNNFILLEEQLIKKSOOKRRTSPSNFKVRF hTKT (L10717)
1
1
       FVLTKTNLSYYE - - YDKMKRGSRKGSIEIK MKK2 aa
FLLTVHKLSYYEYDFERGRRGSKKGSIDVE hAtk (X58957)
FVLTKASLAYFEDR - - HGKKRTLKGSIELS hTKT (L10717)
31
31
4
       KIRCVEKVNLEEQTPVERQ------ MKK2 aa
KITCVETVVPEKNPPPEROIPRRGEESSEM hAtk (X58957)
59
60
        RIKC V E I V K S D - - - - - - - - - - - hTKT (L10717)
59
                                                                                                                                   mTec (X5663)
4
        78
98 SRSOWLKALOKEIRGNPHLLVKYHSGFFVD MKK2 aa
120 LRKRWIHOLKNVIRYNSDLVQKYHPCFWID hAtk (X58957)
98 SRORWVLALKEETRNNNSLVPKYHPNFWMD hTKT (L10717)
17 SRDRWVKKLKEETKNNNNIMIKYHPKFWAD mTec (X5663)
128 G K F L C C Q Q S C K A A P G C T L W E A Y A N L H T A V N MKK2 aa
150 G Q Y L C C S Q T A K N A M G C Q I L E N R N G S L K P G S hAtk (X58957)
126 G K W R C C S Q L E K L A T G C A Q Y D - - - - - - - P hTKT (L10717)
47 G S Y Q C C R O T E K L A P G C E K Y N L F E S S I - - - mTec (X5663)
150 E E K H R V PT F P D R V L K I P R A V P V L K M D A P S S MKK2 aa
180 S H R K T K K P L P P - - - - T P E E D Q I L K K P L P P E hAtk (X58957)
149 T K N A S K K P L P P - - - - T P E D N R - - - - - - hTKT (L10717)
73 5 - - - - - R K T L P P - - - - A P E - - - - I K K R R P P - mTec (X5663)
188 S T T L A Q Y DN E S K K N Y G S Q P P S S S T S L A Q Y D MKK2 aa
206 P A A P V S T S E L K K - - - - - - - - - V V A L Y D hAtk (X58957)
166 - - - R P L W E P E E T V - - - - - - - - - V I A L Y D hTKT (L10717)
89 P P I P P E E N T E E I - - - - - - - V V A M Y D mTec (X5663)
218 SNSKKIYGSQPNFNMQYIPREDFP-DWWQV MKK2 aa
225 YMPMNANDLOLRKGDEYFILEESNLPWWRA hAtk (X58957)
182 YQTNDPQELALRRNEEYCLLDSSEIHWWRV hTKT (L10717)
108 FOATEAHDLRLERGQEYIILEKNDLHWWRA mTec (X5663)
 247 RKLKSSSSSEDVASSNQKERNVNHTTSKIS MKK2 aa
255 RD - - KNGQEGYIPSNYVTE - A - - - - - - - - - hAtk (X58957)
212 QD - - RNGHEGYVPSSYLVEKS - - - - - - - - hTKT (L10717)
138 RD - - K - - - - - - - - - - - - - - mTec (X5663)
 307 EQLLRQKGKEGAFMVRNSSOVGMYTVSLFS MKK2 aa
292 EQLLKQEGKEGGFIVRDSSKAGKYTVSVFA hAtk (X58957)
250 EKLLLDTGKEGAFMVRDSRTAGTYTVSVFT hTKT (L10717)
154 EOLLRTEDKEGGFMVRDSSOPGLYTVSLYT mTec (X5663)
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337 K - AVNDKKGTVKHYHVH - - TNAENKLYLAE MKK2 aa
322 K ST - G D P Q G V I R H Y V V - - C ST P Q S Q Y Y L A E hAtk (X58957)
280 K A V V S E N N P C I K H Y H I K E T N D N P K R Y Y V A E hTKT (L10717)
184 K F G - G E G S S G F R H Y H I K E T A T S P K K Y Y L A E mTec (X5663)
364 NYCFDSIPKLIHYHQHNSAGMITRLRHPVS MKK2 aa
349 KHLFSTIPELINYHQHNSAGLISRLKYPVS hAtk (X58957)
310 KYVFDSIPLLINYHOHNGGGLVTRLRYPVC hTKT (L10717)
213 KHAFGSIPEIIEYHKHNAAGLVTRLRYPVS mTec (X5663)
394 TKANKVPDSVSLGNGIWELKREEITLLKEL MKK2 aa
379 QQNKNAPSTAGLGYGSWEIDPKDLTFLKEL hAtk (X58957)
340 FGRQKAPVTAGLRYGKWVIDPSELTFVQEI hTKT (L10717)
243 TKGKNAPTTAGFSYDKWEINPSELTFMREL mTec (X5663)
 424 GSGQFGVVQLGKWKGQYDVAVKMIKEGSMS MKK2 aa
409 GTGQFGVVKYGKWRGQYDVAIKMIKEGSMS hAtk (X58957)
370 GSGOFGLVHLGYWLNKDKVAIKTIREGAMS hTKT (L10717)
273 GSGLFGVVRLGKWRAQYKVAIKAIREGAMC mTec (X5663)
  454 E DEFFOE AOTMMKLSHPKLVKFYGVCSKEY MKK2 aa
439 E DEFIEE A KVMMNLSHEKLVQLYGVCTK QR hAtk (X58957)
400 E E D F I E E A E V M M K L S H P K L V Q L Y G V C L E Q A hTKT (L10717)
303 E E D F I E E A K V M M K L T H P K L V O L Y G V C T Q O K mTec (X5663)
  484 PIYIVTEYISNGCLLNYLRSHGKGLEPSQL MKK2 aa
469 PIFIITEYMANGCLLNYLREMRHRFQTQOL hAtk (X58957)
430 PICLVFEFMEHGCLSDYLRTQRGLFAAETL hTKT (L10717)
333 PIYIVTEFMERGCLLNFLRQRQGHFSRDML mTec (X5663)
   514 LEMCYDVCEGMAFLESHQFIHRDLAARNCL MKK2 aa
499 LEMCKDVCEAMEYLESKOFLHRDLAARNCL hAtk (X58957)
460 LGMCLDVCEGMAYLEEACVIHRDLAARNCL hTKT (L10717)
363 LSMCQDVCEGMEYLERNSFIHRDLAARNCL mTec (X5663)
   VDRDLCVKVSDFGMTRYVLDDQYVSSVGTK MKK2 aa

VNDQGVVKVSDFGLSRYVLDDEYTSSVGSK hAtk (X58957)

490 VGENQVIKVSDFGMTRFVLDDQYTSSTGTK hTKT (L10717)

393 VNEAGVVKVSDFGMARYVLDDQYTSSSGAK mTec (X5663)
    574 F P V K W S A P E V F H Y F K Y S S K S D V W A F G I L M W MKK2 aa
559 F P V R W S P P E V L M Y S K F S S K S D I W A F G V L M W hAtk (X58957)
520 F P V K W A S P E V F S F S R Y S S K S D V W S F G V L M W hTKT (L10717)
423 F P V K W C P P E V F N Y S R F S S K S D V W S F G V L M W mTec (X5663)
     604 EVFSLGKOPYDLYDNSQVVLKVSQGHRLYR MKK2 aa
589 EIYSLGKMPYERFTNSETAEHIAOGLRLYR hAtk (X58957)
550 EVFSEGKIPYENRSNSEVVEDISTGFRLYK hTKT (L10717)
453 EIFTEGRMPFEKNTNYEVVTMVTRGHRLHR mTec (X5663)
      PHLASDTIYOIMYSCWHELPEKRPTFQQLL MKK2 aa
619 PHLASEKVYTIMYSCWHEKADERPTFKILL hAtk (X58957)
580 PRLASTHVYOIMNHCWKERPEDRPAFSRLL hTKT (L10717)
483 PKLATKYLYEVMLRCWQERPEGRPSFEDLL mTec (X5663)
                                                                                                                                                                            MKK2 aa
       664 SSIE PLREKDKH
                                                                                                                                                                            hAtk (X58957)
       649 SNILDVMDEES
610 ROLAEIAES --- GL
513 RTIDE LVECEET FGR
                                                                                                                                                                            hTKT (L10717)
                                                                                                                                                                             mTec (X5663)
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MSNICQRLWE------KLTEERDGSLNQ-ShFyn
MGCVQCKDKEA-T---KLTEERDGSLNQ-ShFyn
MGCVHCKEKIS-G---KGQGGSGTGTPA-H cYrk
MGSNKSKPKDA-SQR-RRSLEPAENVHG-A hSrc
MGCIKSKENKS-PAI-KYRPENTPEPVS-T hYes
MGCVFCKKLEP-VATAKEDAGLEGDFRSYG hFgr
MGCIKSKGKDSLSDDGVDL-KTQPVRNTER hLyn
MGSMKSK---FLQVGGNTFSKTETSASPHC hHck
MGCGCSS-----HPEDDWMENIDVCENCHY hLck
MGLLSSKRQVSEKGKGWSPVKIRTQDKAPP mBlk
                                                                                                                                                       MKK3 MPI aa
1
1
1
1
1
1
1
                                                                                                                         ---Y L <u>E P</u> MKK3 MPI aa
        SGYRYGTDPTPQHYPSFGVTSIPN--YNNFhFynPPSQYDPDPT-OLSGAF--THIPD--FNNFCYrkGGGAFPASOTPSKPASADGHRGPSAAFAPAhSrcSVSHYGAEPTTVSPCPSSSAKGTAVNFSSLhYesAADHYGPDPTKARPAS-SFAHIPN--YSNFhFgrTIYVRDPTSNKOQRPVPESQLLPGQRFQTKhLynPVYVPDPTSTIKPGPNSHNSNTPGIR----hHck
11
26
26
28
28
 30
 30
 28
          PIVPLDGKGTLLIRNGSEVRD-PLVTYEGS hLck
 26
          PLPPLVVFNHLAPPSPNQ-----
 31
          15
54
51
58
  58
  57
  60
  54
55
  49
                               ---YFVALFDYQARTAEDLSFRAGDK MKK3 MPI aa
            H - - - - - YF V A LFD Y Q A R TA E D L S F R A G D K MKK3
R G G T G V T L F V A L Y D Y E A R T E D D L S F H K G E K hFyn
I T G G G V T L F T A L Y D Y E A R T E D D L S F Q K G E K CYRk
P L A G G V T T F V A L Y D Y E S R T E T D L S F K K G E R hSrc
G L T G G V T T F V A L Y D Y E A R T T E D L S F K K G E R hYes
V S G I G V T L F T A L Y D Y E A R T E D D L T F T K G E K hFgr
- - - - - D I V V A L Y P Y D G I H P D D L S F K K G E K hLyn
- - - - - - I I V V A L Y D Y E A I H H E D L S F Q K G D Q hHck
- - - - - R F V V A L F D Y A A V N D R D L Q V L K G E K mBlk
 45
 79
 78
  81
  88
   74
   66
   60
   64
   55
   69 LOVLDTLHEGWWFARHLEKRRDGSSQQLQG MKK3 MPI aa
109 FOILNSSEGDWWEARSLTTGETG----- hFyn
108 FHIINNTEGDWWEARSLSSGATG----- CYRK
111 LQIVNNTEGDWWLAHSLSTGQTG----- hSrc
118 FOIINNTEGDWWEARSIATGKNG----- hYes
104 FHIINNTEGDWWEARSIATGKNG----- hYes
```

FIGURE 11A

```
Y I P S N Y V A E D R S L Q A E P W F F G A I G R S D A E K MKK3 MPI aa
       YIPSNYVAPVDSIQAEEWYFGKLGRKDAER
132
131 Y I P S N Y V A P V D S I Q A E E W Y F G K I G R K D A E R CYRK
134 Y I P S N Y V A P S D S I Q A E E W Y F G K I T R R E S E R hSrc
141 Y I P S N Y V A P A D S I Q A E E W Y F G K M G R K D A E R hYes
127 CIPSNYVAPVDSIOAEEWYFGKIGRKDAER hfgr
112 FIPSNYVAKLNTLETEEWFFKDITRKDAER hLyn
106 YIPSNYVARVDSLETEEWFFKGISRKDAER hLck
110 FIPFNFVAKANSLEPEPWFFKNLSRKDAER hLck
111 YVPSNFVAPVETLEVEKWFFRTISRKDAER mBlk
      QLLYSENKTGSFLIRESESOKGEFSLSVLD MKK3 MPI aa
       QLLSFGNPRGTFLIRESETTKGAYSLSIRD
161 OLLCHGNCRGTFLIRESETTKGAYSLSIRD
                                                                                                              cYrk
       LLLNAENPRGTFLVRESETTKGAYCLS VSD
LLLNPGNORGIFLVRESETTKGAYSLSIRD
                                                                                                              hSrc
 171
       QLLSPGNPQGAFLIRESETTKGAYSLSIRD
QLLAPGNSAGAFLIRESETLKGSFSLSVRD
 157
                                                                                                              hLyn
 142
       QLLAPGNMLGSFMIRDSETTKGSYSLSVRD hHck
QLLAPGNTHGSFLIRESESTAGSFSLSVRD hLck
 136
 140
 131 OLLAPMNKAGSFLIRESESNKGAFSLSVKD mBlk
               ---GAVVKHYRIKRLDEGGFFLTRRRIF MKK3 MPI aa
 159 - - - - GAVVKHYRIKRL DEGGFF LITRIKH IF
192 W D D M K G D H V K H Y K I R K L D N G G Y Y I T T R A Q F
 191 W DEAKGDHVKHYKIRKLDSGGYYITTRAQF
                                                                                                              cYrk
 194 FDMAKGLNVKHYKIRKLDSGGFYITSRTQF
 201 W D E I R G D N V K H Y K I R K L D N G G Y Y I T T R A Q F

187 W D Q T R G D H V K H Y K I R K L D M G G Y Y I T T R V O F

192 F D P V H G D V I K H Y K I R S L D N G G Y Y I S P R I T F

166 Y D P R Q G D T V K H Y K I R T L D N G G F Y I S P R S T F

170 F D Q N Q G E V V K H Y K I R N L D N G G F Y I S P R I T F
                                                                                                              hFar
                                                                                                              hLyn
                                                                                                               hHck
                                                                                                               hLck
       ITT-OGEVVKHYKIRSLDNGGYYISPRITE mBlk
  184 STLNEFVSHYTKT SDGLCVKLGKPCLKIQV MKK3 MPI aa
222 ETLOQLVQHYSERAAGLCCRLVVPCHKGM - hFyn
221 DTIQQLVQHYIERAAGLCCRLAVPCPKGT - cYrk
224 NSLQQLVAYYSKHADGLCHRLTTVCPTSK - hSrc
231 DTLQKLVKHYTEHADGLCHKLTTVCPTVK - hYes
217 NSVOELVOHYMEVNDGLCNLLIAPCTIMK - hFgr
202 PCISDMIKHYQKQADGLCRRLEKACISPK - hLyn
196 STLQELVDHYKKGNDGLCQKLSVPCMSSK - hHck
200 PGLHELVRHYTNASDGLCTRLSRPCQTQK - hLck
190 PTLQALVOHYSKKGDGLCOKLTLPCVNLA - mBlk
  190 PTLOALVOHYSKKGDGLCOKLTLPCVNLA-
                                                                                                               mBlk
         PAPFDLSYKTVDQWEIDRNSIQLLKRLGSG MKK3 MPI aa
PRLTDLSVKTKDVWEIPRESLQLIKRLGNG hFyn
PKLADLSVKTKDVWEIPRESLQLLQKLGNG CYRK
PQTQGLA---KDAWEIPRESLRLEVKLGQG hSrc
PQTQGLA---KDAWEIPRESLRLEVKLGQG hYes
PQTLGLA---KDAWEISRSSITLERRLGTG hFgr
PQ----KPWDKDAWEIPRESIKLVKRLGAG hLyn
PQ----KPWEKDAWEIPRESLKLEKKLGAG hHck
PQ----KPWWEKDAWEIPRESLKLVERLGAG hHck
PQ----KPWWEDEWEVPRETLKLVERLGAG hLck
PK----NLWAQDEWEIPRQSLKLVRKLGSG mBlk
   214
   251
   250
   253
   260
   246
   231
   225
```

FIGURE 11B

```
QFGEVWEGLWNNTTPVAVKTLKPGSMDPND MKK3 MPI aa
QFGEVWMGTWNGNTKVAIKTLKPGTMSPES hFyn
244
281 Q F G E V W M G T W N G N T K V A L I K T L K P G T M S P E S
280 O F G E V W M G T W N G T T K V A V K T L K P G T M S P E A
280 C F G E V W M G T W N G T T R V A I K T L K P G T M S P E A
287 C F G E V W M G T W N G T T K V A I K T L K P G T M M P E A
273 C F G D V W L G T W N G S T K V A V K T L K P G T M S P K A
257 Q F G E V W M G Y Y N N S T K V A V K T L K P G T M S V O A
251 Q F G E V W M G Y Y N G H T K V A V K T M K P G S M S Y E A
255 Q F G E V W M G Y Y N G H T K V A V K S L K Q G S M S P D A
245 O F G E V W M G Y Y K N N M K V A I K T L K E G T M S P E A
281
                                                                                                     cYrk
                                                                                                     hFgr
                                                                                                     hLyn
                                                                                                     hHck
                                                                                                     hLck
274 F LREAQIMKNLRHPKLIQLYAVCTLEDPIY
                                                                                                      MKK3 MPI aa
       FLEEAQIMKKLKHDKLVQLYAVVS
                                                                                  - E E P I Y
                                                                                                      hFyn
      FLEEAQIMKRLRHDKLVQLYAVVS
                                                                                  -EEPIY
                                                                                                      cYrk
 310
      FLQEAQVMKKLRHEKLVQLYAVVS-EEPIY
FLQEAQIMKKLRHDKLVPLYAVVS-EEPIY
                                                                                                      hSrc
 310
                                                                                                      hYes
 317
      FLEEAOVMKLLRHDKLVOLYAVVS-EEPIY
FLEEANLMKTLOHDKLVRLYAVVTREEPIY
FLAEANVMKTLOHDKLVKLHAVVTKE-PIY
FLAEANLMKOLOHORLVRLYAVVT-OEPIY
                                                                                                      hFgr
 303
                                                                                                      hLyn
 287
                                                                                                      hHck
 281
                                                                                                      hLck
 285
 275 FLGEANVMKTLQHERLVRLYAVVTRE-PIX
                                                                                                      mBlk.
        IITELMRHGSLQEYLQNDTGSKIHLTQQVD MKK3 MPI aa
IVTEYMNKGSLLDFLKDGEGRALKLPNLVD hFyn
 304
 340
        IVTEFMSQGSLLDFLKDGDGRYLKLPQLVD
                                                                                                       cYrk
 339
339
        IVTEYMSKGSLLDFLKGETGKYLRLPQLVD
                                                                                                       hSrc
        IVTEFMSKGSLLDFLKEGDGKYLKLPQLVD
                                                                                                       hYes
  346
        IVTEFMCHGSLLDFLKNPEGODLRLPOLVD
IITEYMAKGSLLDFLKSDEGGKVLLPKLID
                                                                                                       hFqr
  332
                                                                                                       hLyn
  317
       IITEFMAKGSLLDFLKSDEGSKOPLPKLID
IITEYMENGSLVDFLKTPSGIKLTINKLLD
IVTEYMARGCLLDFLKTDEGSRLSLPRLID
                                                                                                       hHck
  <u>3</u>10
                                                                                                       hLck
  314
                                                                                                       mBlk
  304
  334 MAAQVASGMAYLESRNYIHRDLAARNVLVG MKK3 MPI aa
       MAAQVAAGMAYIERMNYIHRDLRSANILVG
MAAQIAAGMAYIERMNYIHRDLRAANILVG
MAAQIASGMAYVERMNYVHRDLRAANILVG
  370
                                                                                                       cYrk
  369
        MAAQIADGMAYIERMNYIHRDLRAANILVG
  362 MAAQIADG MAYIERMNYIHRDLRAANILVG Hes

362 MAAQVAEG MAYMERMNYIHRDLRAANILVG hFgr

347 FSAQIAEG MAYIERKNYIHRDLRAANVLVS hLyn

340 FSAQIAEG MAFIEQRNYIHRDLRAANILVS hHck

344 MAAQIAEG MAFIEERNYIHRDLRAANILVS hLck

334 MSAQVAEG MAYIERMNSIHRDLRAANILVS mBlk
   364 EHNIYKVADFGLARVFKVDNEDIYESRHEI MKK3 MPI aa
   400 NGLICKIADFGLARLI - - EDNEYTARQGA hFyn
   400 NGLICKIADFGLARLI --- EDNEYTARQGA hFyn

399 DNLVCKIADFGLARLI --- EDNEYTARQGA CYRK

399 ENLVCKVADFGLARLI --- EDNEYTARQGA hSrc

406 ENLVCKIADFGLARLI --- EDNEYTARQGA hYes

392 ERLACKIADFGLARLI --- KDDEYNPCOGS hFgr

377 ESLMCKIADFGLARVI --- EDNEYTAREGA hLyn

370 ASLVCKIADFGLARVI --- EDNEYTAREGA hHck

374 DTLSCKIADFGLARLI --- EDNEYTAREGA hLck

364 ETLCCKIADFGLARII --- DSEYTAQEGA mBlk
```

FIGURE 11C

```
KLPVKWTAPEAIRSNKFSIKSDVWSFGILL
                                                                             MKK3 MPI aa
    K F P I K W T A P E A A L Y G R F T I K S D V W S F G I L L
427
    K F P I K W T A P E A A L F G K F T I K S D V W S F G I L L K F P I K W T A P E A A L Y G R F T I K S D V W S F G I L L
                                                                             cYrk
426
                                                                   GILL
                                                                             hSrc
426
                                                                   GILQ
            IKWTAPEAALYGRFTIKSDVWSF
         P
                                                                             hyes
433
         PIKWTAPEAALFGRFTIKSDVWSFGILL
PIKWTAPEAINFGCFTIKSDVWSFGILL
419
                                                                             hLvn
404
    K F P I K W T A P E A I N F G S F T I K S D V W S F G I L L
397
                                                                             hHck
401 KFPIKWTAPEAINYGTFTIKSDVWSFGILL hLck
390 KFPIKWTAPEAIHFGVFTIKADVWSFGVLL mBlk
     YEIITYGK MPYSGMTGAQVIQMLAQNYRLP MKK3 MPI aa
    TELVTKGRVPYPGMNNREVLEQVERGYRMP hFyn
457
    TELVTKGRVPYPGMNNREVL<u>E</u>QVERGYRMQ cYrk
456
    TELTTKGRVPYPGMVNREVLDQVERGYRMP
                                                                             hSrc
456
463 TELVTKGRVPYPGMVNREVLEQVERGYRMP hYes
449 TELITKGRIPYPGMNKREVLEOVEQGYHMP hFgr
434 YEIVTYGKIPYPGRTNADVMTALSQGYRMP hLyn
427 MEIVTYGRIPYPGMSNPEVIRALERGYRMP hHck
431 TEIVTHGRIPYPGMTNPEVIQNLERGYRMP hLck
    MVIVTYGRVPYPGMSNPEVIRSLEHGYRMP mBlk
QPSNCPQOFYN-IMLECWNAEPKERPTFET MKK3 MPI aa
487 CPQDCPISLH-ELMIHCWKKDPEERPTFET MKK3 MPI aa
486 CPGGCPPSLH-DVMVQCWKREPEERPTFEY hFyn
486 CPPECPESLH-DLMCOCWRKEPEERPTFEY hSrc
493 CPQGCPESLH-ELMNLCWKKDPDERPTFEY hYes
479 CPPGCPASLY-EAMEQTWRLDPEERPTFEY hFgr
464 RVENCPDELY-DIMKMCWKEKAEERPTFDY hLyn
457 RPENCPEELY-NIMMRCWKNRPEERPTFEY hHck
461 RPDNCPEELY-QLMRLCWKERPEDRPTFDY hLck
450 CPETCPPELYNDIITECWRGRPEERPTFEF mBlk
483 LRWKLEDYFE-TDSSYSDANNFIR
                                                                              MKK3 MPI aa
     LQSFLEDYFTATEPQYQPGEN
                                                                              hFyn
516
     LQSFLEDYFTATEPQYQPG|D|N|---Q
                                                                              cYrk
515
515 LQAFLEDYFTSTEPQYQPGEN - - - L
                                                                              hSrc
      IQSFLEDYFTATEPQYQPGEN
                                                                              hYes
522
     LQSFLEDYFTSAEPQYQPGDQ
                                                                              hFgr
 508
493 L Q SV LD DF YTATEGQY QQ - - Q
486 IOSV LD DF YTATESQY QQ - - Q
490 LRSV LEDFFTATEGQY OP - - Q
                                                                              hLyn
                                                        - - - P
- - - P
                                                                              hHck
                                                                              hLck
             VLEDFYTATEGOYEL
                                                                              mBlk
 480 LO
```

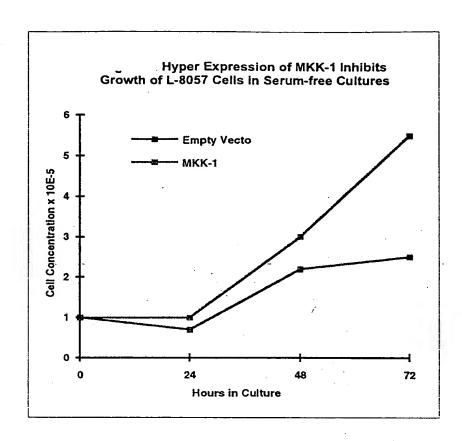


FIGURE 12

Growth Factor Response of MKK-1 Expressing L-8057 Cells

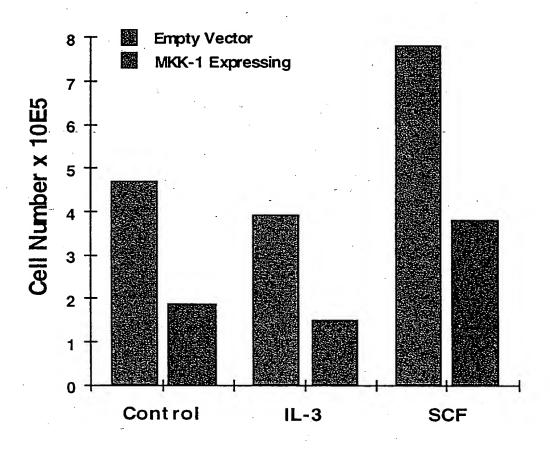


FIGURE 13

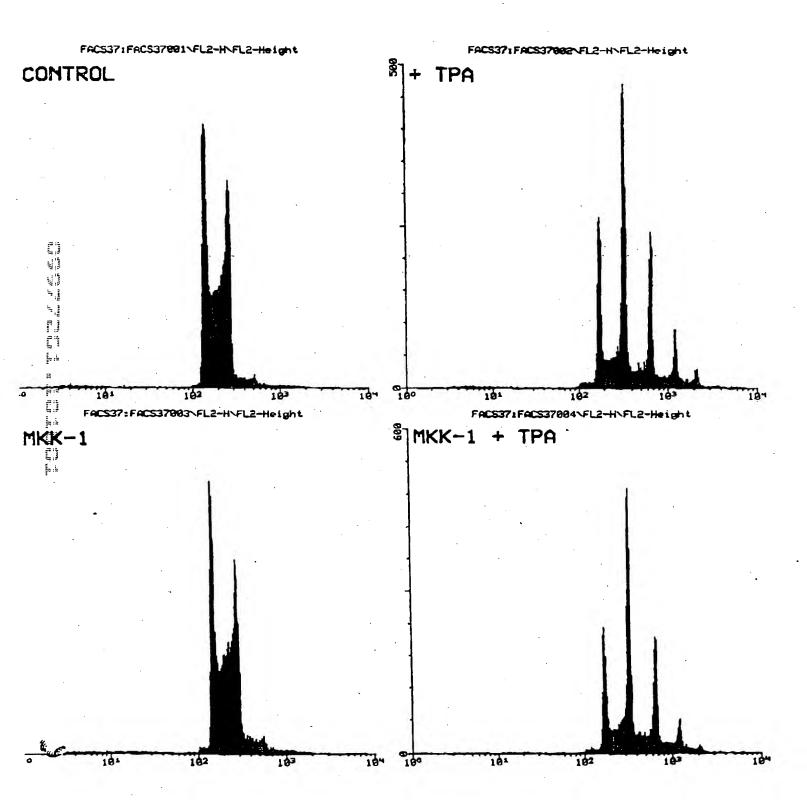


FIGURE 14